## REMARKS

Claim 1 has been amended to recite that in step (6) the asparagine-linked disialooligosaccharide or asparagine-linked monosialooligosaccharide has amino group nitrogen protected with a fat-soluble protective group. The amendment to claim 1 provides proper antecedent basis for the recitation in step (7) of "removing the fat-soluble protective group to form a free amino group" and overcomes the 35 U.S.C. § 112, second paragraph, rejection. Amidating the free amino group and a carboxyl group of the asparagine portion of an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide having amino group nitrogen protected with a fat-soluble protective group as now recited in step (6) of claim 1 is described in, for example, paragraphs [0026] and [0038] of the publication, US 20050222382, of the present application.

Claims 1 and 5-7 are rejected in the Action under 35 U.S.C. § 103(a) as being unpatentable over Meinjohanns et al. (J. Chem. Soc. *Perkin Trans. 1*, Vol. 1, 1998, 549-560) in view of Komba et al. (*J. Peptide Science*, 6; 585-593 (2000)).

The Office identifies Meinjohanns et al. as teaching a method for preparing N-linked glycopeptides by attaching Fmoc-protected amino acid and Fmoc-protected asparagine building blocks. The

Office identifies Komba et al. as teaching the preparation of Sialyl-T-Glycopeptides (O-linked) via Fmoc/OPfp-ester strategy using a sialyl-T building block of which the carboxyl group is protected by a methyl group to avoid cleavage by acids such as TFA. The Office concludes that one of ordinary skill in the art would have applied Komba's technique to Meinjohanns' method and would have expected the modification to be successful.

Applicant respectfully submits that the combination of Meinjohanns et al. and Komba et al. is insufficient to support a *prima facie* case of obviousness of claims 1 and 5-7 (as amended) under 35 U.S.C. § 103(a).

Claim 1 has been amended as noted above to limit the protective group of the carboxyl group of the sialic acid to a benzyl, allyl, or diphenylmethyl group. The carboxyl group protected by these protective groups is much more easily deprotected than that protected by a methyl group as used in Komba's method. A benzyl, allyl, or dephenylmethyl group can be removed under neutral or mild acidic condition, which does not adversely affect the sialic acid. However, the removal of a methyl group needs a basic condition or strong acidic condition. A basic condition increases a risk of racemization of the peptide chain, and a strong acidic condition hydrolyzes deprotected sialic acid.

Neither Meinjohanns et al. nor Komba et al. discloses or

suggests using a benzyl, allyl, or diphenylmethyl group as a protective group of a carboxyl group of a sialic acid, and neither discloses or suggests the remarkable effect provided by these protective groups.

For the above reasons amended claims 1 and 5-7 are not obvious under 35 U.S.C. 103(a) over the combination of Meinjohanns et al. and Komba et al. and the rejection is improper and should be removed.

Claims 22-25 are rejected in the Action under 35 U.S.C. § 103(a) as being unpatentable over Meinjohanns et al. in view of Komba et al. as applied to claims 1 and 5-7, and further in view of Ratcliffe et al., US 5,527,901. The Office identifies Ratcliffe et al. as teaching the use of benzyl ester or phenacyl ester protection as an alternative to methyl ester protection for the carboxyl group of sialic acid and that such the use of these blocking groups give a higher yield of product and higher anomeric purity. The Office concludes that it would have been obvious, in view of Ratcliffe et al., to use benzyl protection in place of methyl protection in the method of Meinjohanns et al. as modified by Komba et al.

However, the technique of Ratcliffe et al. is directed to liquid-phase synthesis of higher sialosides, and is not related to solid-phase synthesis of glycopeptides. The protective group in

Ratcliffe et al. is used for the acid moiety of the sialosyl halide, and is not used for acidic condition for cleavage of glycopeptides from a resin. In addition, Ratcliffe et al. suggests that the blocking group is removed before coupling of the sialoside to proteins and insoluble carriers (see Col. 3, lines 3-8), which means that the protective group is not used during the solid-phase synthesis of glycopeptides.

Based on the above, Ratcliffe et al. would have been considered by one of ordinary skill in the art to relate to a different technical field than that of the present invention (and that of Meinjohanns et al. and Komba et al.) and the person of ordinary skilled in the art would not have been motivated or have had any other reason to modify the combination of Meinjohanns et al. and Komba et al. as proposed in the Action.

For the above reason, the combination of Meinjohanns et al., Komba et al. and Radcliffe et al. does not support the 35 U.S.C. § 103(a) rejection of claims 22-25 and the rejection is improper and should be removed.

Furthermore, it is noted that the present invention provides an addition effect that is remarkable and unexpected. The inventor of the present invention found that the carboxyl group of the sialic acid is selectively protected by a protective group when adjusting pH to a mild acidic to neutral condition after Fmoc

protection of amino group nitrogen of the asparagine portion of asparagine-linked oligosaccharide. Under this condition, the carboxyl group of asparagine is not protected by benzyl group (see compound (12) on page 32 of the present specification), and the product can be used as it is for amidating with free amino group of synthesized oligopeptide. (Please refer to Reference Example 3 in the present specification). When pH does not fall within this range, the carboxyl group of the asparagine will also be protected with the benzyl group, and cannot be subjected to the amidating process.

None of the prior art discloses asparagine-linked oligosaccharide having its hydroxyl group(s) of sialic acid(s) selectively protected and none discloses the method of obtaining it. Therefore, one of ordinary skilled in the art could not have thought of the present invention, especially step (6), based on the cited references.

The foregoing is believed to be a complete and proper response to the Office Action dated November 7, 2008, and is believed to place this application in condition for allowance. If, however, minor issues remain that can be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number indicated below.

In the event that this paper is not considered to be timely filed, applicant hereby petitions for an appropriate extension of time. The fee for any such extension may be charged to our Deposit Account No. 111833.

In the event any additional fees are required, please also charge our Deposit Account No. 111833.

Respectfully submitted,

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